IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

INVITAE CORPORATION, Plaintiff, v. NATERA, INC., Defendant.	Civil Action No. 21-669-GBW
INVITAE CORPORATION, Plaintiff, v. NATERA, INC., Defendant.	Civil Action No. 21-1635-GBW

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MEMORANDUM OPINION

October 18, 2022
Wilmington, Delaware

GREGORY B. WILLIAMS
UNITED STATES DISTRICT JUDGE

In these two actions filed by Plaintiff Invitae Corporation ("Invitae") against Defendant Natera, Inc. ("Natera"), Invitae alleges infringement of United States Patent Nos. 10,604,799 ("'799 patent"), 11,149,308 ("'308 patent"), and 11,155,863 ("'863 patent"). All three patents share a common written description.

Presently before the Court is the issue of claim construction of multiple terms in the '799 patent, the '308 patent, and the '863 patent. The Court has considered the parties' joint claim construction brief. C.A. No. 21-669, D.I. 72; C.A. No. 21-1635, D.I. 49. The Court held a *Markman* hearing on October 4, 2022 ("Tr. __").

I. BACKGROUND

On May 7, 2021, Invitae filed its Complaint alleging that Natera infringes the '799 patent. C.A. No. 21-669, D.I. 1. On November 21, 2021, in a separate action, Invitae filed its Complaint alleging that Natera also infringes the '308 patent and the '863 patent. C.A. No. 21-1635, D.I. 1. The asserted patents generally relate to the field of sequence assembly. The claimed invention enables the identification of mutations with positional accuracy in a computationally tractable way. The asserted patents provide a summary of the claimed invention:

> Methods of the invention are accomplished by assembling contigs from sequence reads, aligning the contigs to a reference sequence, aligning the reads back to the contig, and identifying mutations via the assembled contig and the alignments. By assembling reads into contigs as well as aligning the individual reads to the contigs, the need to compare each of the reads to all of the others is avoided, providing computational tractability even for very high throughput analyses.

'799 patent at 2:35-43.

II. LEGAL STANDARDS

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (internal quotation marks omitted); *see also Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989) ("A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using, or selling the protected invention."). "[T]here is no magic formula or catechism for conducting claim construction." *Phillips*, 415 F.3d at 1324. The Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.* The ultimate question of the proper construction of a patent is a question of law, although subsidiary fact-finding is sometimes necessary. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (quoting *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996)).

"The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (citing *Phillips*, 415 F.3d at 1312–13). A person of ordinary skill in the art "is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips*, 415 F.3d at 1313.

"When construing claim terms, [the court] first look[s] to, and primarily rely[s] on, the intrinsic evidence, including the claims themselves, the specification, and the prosecution history of the patent, which is usually dispositive." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1276 (Fed. Cir. 2013) (internal quotation marks and citations omitted). "Other

claims of the patent in question, both asserted and unasserted, can . . . be valuable" in discerning the meaning of a disputed claim term because "claim terms are normally used consistently throughout the patent," and so, "the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Phillips*, 415 F.3d at 1314. In addition, "[d]ifferences among claims can also be a useful guide[.]" *Id.* For example, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15.

In addition to the claim, the Court should analyze the specification, which "is always highly relevant to the claim construction analysis ... [as] it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316 (citation omitted). "[E]ven when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)). And, the specification "is not a substitute for, nor can it be used to rewrite, the chosen claim language." *SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004).

The Court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370, (1996). The prosecution history "can often inform the meaning of the claim language by

demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution[.]" *Phillips*, 415 F.3d at 1317.

In some cases, the Court "will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. "Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. Overall, while extrinsic evidence may be useful, it is "less significant than the intrinsic record in determining the legally operative meaning of claim language." *Phillips*, 415 F.3d at 1317 (internal quotation marks and citations omitted).

III. AGREED UPON TERM

The parties agreed upon the construction of claim term "genotyping" in the '308 patent to mean "assigning a genotype to." D.I. 57-1 at 45.[1] The Court will adopt the agreed-upon construction of "genotyping."

IV. CONSTRUCTION OF DISPUTED TERMS

A. "sequence reads"

The claim term "sequence reads" appears in certain claims of all three asserted patents. The parties' competing proposed constructions for "sequence reads" are set out in the chart below:

Claim Term	Plaintiff Invitae's Construction	Defendant Natera's Construction
"sequence reads"	"[m]easurements by a sequencer of the order of bases in a polynucleotide"	"[r]aw, unaligned reads as generated by the sequencing instrument"

[1] Unless otherwise noted, references to docket cites refer to C.A. No. 21-669.

The parties dispute whether the term "sequence reads" excludes pre-processing or pre-alignment of the sequence reads prior to being entered into a computer system and used in the assembly and alignment steps. *See* D.I. 72 at 10-27; D.I. 80 at 1, 2. For the reasons set out below, the Court construes the claim term "sequence reads" to mean "raw reads as generated by the sequencing instrument."

The use of the disputed terms in claim 1 of the '799 patent is representative.

> 1. A method for assembling ***sequence reads***, the method comprising:
>
> obtaining a sample comprising template nucleic acid;
>
> sequencing the template nucleic acid to generate a plurality of ***sequence reads***;
>
> inputting a reference genome and said plurality of ***sequence reads*** into a computer system comprising a processor coupled to a non-transitory memory to perform the steps of:
>
> assembling a contig from at least some of the plurality of ***sequence reads***;
>
> identifying a plurality of contig:reference descriptions of mutations by aligning the contig to said reference genome;
>
> identifying a plurality of read:contig descriptions by aligning each of the plurality of ***sequence reads*** to the contig; and
>
> combining the contig:reference descriptions with the read:contig descriptions to produce read:reference descriptions to map positional information of mutations found in the individual reads relative to the reference.

'799 patent at claim 1 (emphases added).

Natera argues that once the sequence reads are generated by a sequencer, they are inputted into a computer, without any additional processing steps between when the sequence reads were generated by the sequencer and inputted into the computer. D.I. 72 at 16. The written description states:

> After aligning each raw read, the alignment of the read to the contig is used to map positional information and any identified differences (i.e., variant information) from the reference to the raw read. The raw read is then translated to include

> positional and variant information, allowing genotyping to be performed using the aligned translated reads.

'799 patent at 2:45-51.

During oral argument, Natera argued "[w]hat the patent tells you is you take the raw reads from the sequencer, you put them into the computer, you make contigs out of them and you compare them to the contig and to the reference inferentially." Tr. at 33. In other words, Natera asserts that the claim term "sequence reads" do not include any pre-processing or pre-alignment steps performed between sequencing and the claimed manipulation of those reads. D.I. 72 at 16. The Court agrees with Natera.

Invitae asserts that, because the claims use the transition term "comprising," there can be additional unrecited steps between the generation of the sequence reads and the assembly of the contigs. *See Amgen Inc. v. Amneal Pharms. LLC*, 945 F.3d 1368, 1378-79 (Fed. Cir. 2020) ("The term 'comprising' is the standard transition term used to make clear that the claim does not preclude the presence of components or steps that are in addition to, though not inconsistent with, those recited in the limitations that follow."); *see also* Tr. at 23. Natera does not dispute Invitae's argument that the term "comprising" means the invention includes but is not limited to the elements identified in the claim. *See* Tr. at 39. Natera, however, correctly points out that "you still have to read [the claims] in light of the specification." *Id.* The asserted patents' written description consistently states that the sequence reads are generated by a sequencer, and they are put into a computer in their raw form. *See, e.g.*, '799 patent at 2:45-51 ("After aligning each raw read, the alignment of the read to the contig is used to map positional information and any identified differences (i.e., variant information) from the reference to the raw read. The raw read is then translated to include positional and variant information[.]"), *id.* at 3:14-16 ("[T]he full set of raw reads can be organized into subsets."), *id.* at 4:19-20 ("With the contigs aligned, each raw

read is aligned to a contig."), *id.* at 4:29-35 ("Each raw read-to-contig alignment is mapped to the reference . . . positional and variant information relative to the reference is provided for each read, allowing each raw read alignment to be translated."), *id.* at 12:37-40 ("The raw reads are aligned to the [] contigs."), *id.* at 12:54-56 ("In step 3, raw reads are aligned to contigs."), *id.* at 12:57-59 ("[R]aw read alignments are mapped from contig space to original reference space."), *id.* at 25:14-18 ("The local, contig-specific alignment of each raw read is determined."), *id.* at 25:31-39 ("For each raw read, any difference between that read and contig to which it has been aligned is identified . . . [S]ome differences between a raw read and a contig will be evidence of rare alleles."), *id.* at 25:41-42 ("The alignments of the raw reads to the contigs are converted."), *id.* at Example 1, Table 2 ("Map of raw read alignments from contig space to original reference space."). Figure 2 in the asserted patents is also instructive. Step three recites, "[a]lign raw reads to contigs." '799 patent at Fig. 2. As noted by Natera during oral argument, "[t]hat [step] happens in the computer. The only way that can happen is if the raw reads went into the computer[.]" Tr. at 33. The Court agrees with Natera.

Invitae also argues that pre-alignment steps are within the scope of the claims because dependent claims 2 and 3 of the '799 patent recite using pre-processing steps, like using barcode sequences,[2] to group reads into subsets. *See* '799 patent at claims 2 and 3 ("The methods of claim 1, further comprising attaching barcode sequences to the template nucleic acid [and] [t]he method of claim 2, further comprising assigning the reads to subsets based on the bardcode sequences."). The Court's construction is consistent with dependent claims 2 and 3 of the '799 patent. The steps

[2] DNA samples can be labeled by attaching a short sample specific nucleotide sequence—a barcode—to each DNA sample prior to sequencing. After sequencing, the DNA samples can easily be identified by the barcode sequence within each sequence read. *See* '799 patent at 3:26-42.

described in dependent claims 2 and 3 of the '799 patent occur *before* the sequence reads are generated. The Court's construction does not exclude those steps.

The Court rejects Natera's use of the word "unaligned" in its proposed construction. The word does not appear in the written description of the asserted patents and the Court finds no support in the intrinsic or extrinsic evidence to include the word "unaligned" in the construction of the claim term "sequence reads."

For the above reasons, the Court construes the claim term "sequence reads" to mean "raw reads as generated by the sequencing instrument."

B. The "plurality of sequence reads" terms

The '308 patent uses the claim term "the sequence reads," while the '799 patent and the '863 patent use the claim term "plurality of sequence reads" (collectively, the "plurality of sequence reads" terms). The parties appear to agree that the terms should be construed consistently, and the Court will do the same. *See* D.I. 72 at 28-47. The parties' competing proposed constructions for the plurality of sequence reads terms are set out in the chart below:

Claim Term	Plaintiff Invitae's Construction	Defendant Natera's Construction
a plurality of sequence reads (the '799 patent) the plurality of sequence reads (the '863 patent) the sequence reads (the '308 patent)	"'[s]equence read' to be defined as above, no other construction necessary."	"[a]ll of the 'sequence reads' generated from the sequencing step (step 1[b] [3])."
said plurality of sequence reads (the '799 patent) the plurality of sequence reads (the '799 patent)	"'[s]equence read' to be defined as above, no other construction necessary."	"[t]he 'plurality of sequence reads' generated in the sequencing step (step 1[b])."

The parties dispute whether the plurality of sequence reads terms mean all of the sequence reads generated in the sequencing step or can mean only some of the sequence reads generated. For the reasons set out below, the Court adopts the construction of "sequence reads" as described above and concludes no additional construction is necessary for the plurality of sequence reads terms.

Natera alleges that basic grammar and claim construction principles support its construction that the plurality of sequence reads terms mean all of the sequence reads generated by the sequencing instrument. Natera explains that "[i]t is the plurality of sequence reads initially generated by the sequencing instrument that provides the antecedent basis for each of those later

[3] The claims in the asserted patents are not numbered. Natera assigned numbers to the steps in the asserted claims "[f]or clarity and the Court's convenience." D.I. 72 at 12 n.2. Natera attached an exhibit to its claim construction briefing that charts the claim elements and assigns alphanumeric notations. *See* D.I. 73 at A0443. "What Natera calls Step 1[b], Invitae calls 'the sequencing step.'" D.I. 72 at 12 n.2.

terms, and nothing in that claim suggests that the 'a plurality' is anything other than all of the reads generated in the sequencing step of the process." D.I. 72 at 34 (citations omitted). The Court disagrees. Natera cites to *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338 (Fed. Cir. 2008) and *TomTom, Inc. v. Adolph*, 790 F.3d 1315 (Fed. Cir. 2015) for the proposition that the word "the" and "said" are "anaphoric phrases referring to the initial antecedent phrase." *See* D.I. 72 at 34 (citations omitted). But, as noted by Invitae, these cases only establish that there is a single "plurality of sequence reads" used throughout the claims. D.I. 72 at 42. These cases do not establish that "plurality" must include all of the sequence reads that are generated by the sequencing instrument. *Id.*; *see also Baldwin*, 512 F.3d at 1343; *TomTom*, 790 F.3d at 1329.

Nothing in the claims or specification require the plurality of sequence reads terms to mean *all* of the sequence reads generated in the sequence step. The preamble of claim 1 of the '308 patent recites, "[a] method for accurately identifying differences between a reference human genome and sequence reads obtained from a biological sample[.]" '308 patent at claim 1. The claim then recites, "sequencing, by next generation sequencing, the nucleic acid to generate the sequence reads[.]" *Id.* The claim language requires the sequence reads to be generated by "next generation sequencing," but does not require that all the sequence reads that are generated are used in the subsequent claimed steps. Similarly, claim 1 of the '799 patent recites, "sequencing the template nucleic acid to generate a plurality of sequence reads." The claim then recites, "assembling a contig from at least some of the plurality of sequence reads." The "at least some language" indicates that the contigs are assembled by all or any subset of the sequencing reads that are generated by a sequencing instrument so long as a "plurality" of sequence reads are used.

For the above reasons, the Court adopts Invitae's construction of "sequence reads" as described above and concludes no construction is necessary for the plurality of sequence reads

terms. *See generally Thorner*, 669 F.3d at 1365 ("The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history.").

C. "contig:reference descriptions of mutations," "contig-to-reference descriptions of mutations," "reference alignment," "read:contig descriptions," "read-to-contig descriptions," "sequence read alignments," "read:reference descriptions," and "read-to-reference descriptions"

The '799 patent uses colons for the following claim terms "contig:reference descriptions of mutations," "read:contig descriptions," and "read:reference descriptions," while the '863 patent uses "-to-'" for the following claim terms "contig-to-reference descriptions of mutations," "read-to-contig descriptions," and "read-to-reference descriptions." The parties appear to agree that the terms should be construed consistently and that there are no substantive differences based on the use of a colon or "-to-" and the Court will do the same. D.I. 72 at 48-49, 66 n.1.

The parties first dispute where to parse the claims of the '799 patent and the '863 patent. Invitae provides a construction for "contig:reference descriptions of mutations," whereas Natera argues that the Court should construe the claim term without the language "of mutations." *See id.* at 66-67. The Court agrees with Invitae that the claim term with the language "of mutations" should be construed.

Natera contends that "descriptions of mutations" appears once in claim 1 of the '799 patent and the '863 patent, while "descriptions" appears throughout the patent and therefore "should receive a construction applicable to all of its uses." *Id.* at 84. Natera further explains that "[t]he reason that [the patents] specifie[] 'contig:reference descriptions of mutations' is that the claim is practiced only where there *is* a difference between the contig and the reference." *Id.* at 66-67. Invitae rebuts Natera's arguments by stating that the claims refer not just to "contig:reference descriptions" but also "contig:reference descriptions of mutations." *Id.* at 75-76. Invitae also

points out that Natera's request to construe the claim term "contig:reference description" without the language "of mutations" "makes little sense" in light of Natera's proposed construction which lists various types of mutations. *Id.* at 75. Natera's proposed construction would introduce redundancy into the claims and render the "of mutation" language in the claims meaningless. The Court agrees with Invitae that, if it adopted Natera's construction, it would render the language "of mutations" redundant, which is disfavored. *See, e.g., Chalumeau Power Sys. LLC v. Alcatel–Lucent,* No. 11-1175-RGA, 2013 WL 5913849, at *4 (D. Del. Oct. 30, 2013) (rejecting proposed construction of claim term "type of device" where the proposed construction rendered language in a later portion of the claim "redundant"). For the above reasons, the Court will construe the claim term "contig:reference descriptions of mutations."

Next, the Court will address the merits of each of the parties' proposed constructions set out in the chart below:

Claim Term	Plaintiff Invitae's Construction	Defendant Natera's Construction
contig:reference descriptions of mutations (the '799 patent) contig-to-reference descriptions of mutations (the '863 patent)	"[a] description of a mutation in a contig as it exists in the nucleic acid with reference to the genome."	"Natera believes that the terms in need of construction are 'contig:reference descriptions' and 'contig-to-reference descriptions,' which mean: 'Information including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases in the contig relative to the reference, such as a CIGAR string.'"
reference alignment (the '308 patent)	"[p]lacement in a reference genome."	"[i]nformation including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases in the contig relative to the reference, such as a CIGAR string"
read:contig descriptions (the '799 patent) read-to-contig descriptions (the '863 patent)	"[a] description of a sequence read with reference to a contig."	"[i]nformation including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases in each sequence read relative to the contig, such as a CIGAR string"
sequence read alignments (the '308 patent)	"[p]lacements of sequence reads."	"[i]nformation including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases in each sequence read relative to the reference, such as a CIGAR string"
read:reference descriptions (the '799 patent) read-to-reference descriptions (the '863 patent)	"[d]escription of a sequence read with reference to the reference genome.'	"[i]nformation including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases in each sequence read relative to the reference, such as a CIGAR string"

For the claim terms "contig:reference descriptions of mutations," "read:contig descriptions," and "read:reference descriptions," Natera proposes nearly identical constructions. Natera argues that the asserted patents describe "the output of the alignment steps, *i.e.*, the

'descriptions,' as positional and variant information." D.I. 72 at 70; *see, e.g.*, '799 patent at 2:30-58 (" . . . Information about the variants in the sample is identified through the alignment of the contigs to the reference . . . [T]he alignment of the read to the contig is used to map positional information and any identified differences . . . allowing genotyping to be performed using the aligned translated reads."). Natera also contends that the asserted patents consistently use CIGAR string. D.I. 72 at 70; *see, e.g.*, '799 patent at 4:15-18 ("In certain embodiments, a computer program creates a file or variable containing a description of the mutation (e.g., a compact idiosyncratic gapped alignment report (CIGAR) string).").

Invitae, on the other hand, argues that the patentee has defined the disputed terms. Invitae points to the specification, which recites:

> Each mutation identified here in a contig or consensus sequence can be described as it exists in the nucleic acid with reference to the reference genome. *For convenience, this could be referred to as a contig:reference description of a mutation.*

'799 patent at 20:35-39 (emphasis added).

> Each read represents a portion of the nucleic acid from the sample that can be described with reference to the contig. *For convenience's sake, this could be referred to as a read:contig description.*

Id. at 21:5-8 (emphasis added).

Invitae also argues that Natera's construction requires "information including the position and the existence of matches, mismatches, deletions, and/or insertions" but "nothing in the claim term requires actual identification of a mutation or any other attributes." D.I. 72 at 50-51. Identification of mutations are recited in the dependent claims. *See, e.g.*, '799 patent at claim 8 ("The method of claim 1, further comprising *identifying* a mutation based on the alignments to the contig and the reference sequence.") (emphasis added). Invitae contends that, if the Court adopts Natera's proposed construction, it would render dependent claim 8 of the '799 patent superfluous.

D.I. 72 at 76-77. Natera responds that there is no claim differentiation problem. Natera asserts that claim 1 of the '799 patent provides information about the existence and position of matches, mismatches, deletion, and/or insertions for the bases in a sequence read relative to the reference. Dependent claim 8 of the '799 patent requires the additional step of identifying the mutations, i.e., which nucleotide is substituted for which. D.I. 72 at 69-70.

The Court agrees with Invitae that there is no requirement that "contig:reference descriptions of mutations," "read:contig descriptions," and "read:reference descriptions" include the position and variant information stated in Natera's proposed construction. Natera's construction improperly narrows these claim terms by its use of the word "existence" in its proposed constructions. Natera's proposed construction requires "contig:reference descriptions of mutations," "read:contig descriptions," and "read:reference descriptions" claim terms to not only include information about the mutation but also the position and the type of mutation. The intrinsic evidence does not support Natera's proposed constructions.

Natera's proposed constructions render dependent claim 8 of the '799 patent superfluous. Natera contends that dependent claim 8 of the '799 patent requires an "additional step" to identify which nucleotide is substituted for which. D.I. 72 at 69-70. But, one must know which nucleotide is substituted for which to know anything about "the position and the existence of matches, mismatches, deletions, and/or insertions." For the above reasons, the Court will adopt Invitae's proposed constructions for the following claim terms: "contig:reference descriptions of mutations," "read:contig descriptions," and "read:reference descriptions."

For the claim terms "reference alignment" and "sequence read alignments," Natera proposes nearly identical constructions. Natera alleges that the specification treats "alignment" and "descriptions" interchangeably; thus, Natera proposes the same construction for all

"description" and "alignment" terms. Natera points to the claim language in the '308 patent, which recites combining "the reference alignment and the sequence read alignments to determine an identity of each of the multiple mutations and its location in the human reference genome." '308 patent at claims 1, 20. Natera argues that it would be impossible to combine the "reference alignment" and the "sequence read alignments" unless these terms included information about the position and the existence of matches, mismatches, deletions, and/or insertions.

Invitae argues that the patentee chose to use different language for its claims in the '308 patent. Thus, there is no basis for claim terms that use different language to be given identical constructions as proposed by Natera. D.I. 72 at 81-82. Invitae also points to the claims to support its proposed constructions. It states that there is nothing in the claims to require the "alignment" terms to include information about the position and existence of matches, mismatches, deletions, and/or insertions. The claims in the '308 patent recite that the "alignment" terms are "*indicative*" of differences between either the contig and the reference human genome or the sequence reads and the contig. '308 patent at claim 1 (emphasis added). Invitae also argues that the specification supports its proposed construction that the "alignment" terms refer to "placement" of a reference genome or sequence read. *See* D.I. 52-53. The specification states, "[a]lignment, as used herein, generally involves placing one sequence along another sequence, iteratively introducing gaps along each sequence, scoring how well the two sequences match, and preferably repeating for various position along the reference. The best-scoring match is deemed to be the alignment and represents an inference about the historical relationship between the sequences." '308 patent at 16:56-62.

The Court agrees with Invitae. There is a presumption that "different terms in the claims connotate different meanings." *CAE Screenplates Inc. v. Heinrich Fiedler GmbH & Co KG.*, 224

F.3d 1308, 1317 (Fed. Cir. 2000); *see also* Tr. at 83. In the asserted patents, the patentee chose to use different claim terms in its patents. Natera's virtually identical proposed constructions ignore this presumption. The specification supports Invitae's proposed construction that the "alignment" terms refer to a placement of a sequence in a reference. *See, e.g.*, '308 patent at 3:53-67 ("For example, where the bwa-sw algorithm is implemented by BWA, parameters of the alignment are optimized to ensure correct placement of the contig on the overall reference genome."); *id.* at 24:60-61 "[e]ach contig is aligned to a reference genome to determine the genomic position of each contig"); *id.* at 20:33-35 ("Parameters of the alignment are optimized to ensure correct placement of the contig on the overall reference genome, for example, where the bwa-sw algorithm is used."). Nothing in the intrinsic evidence require the "alignment" terms to include information about the position and existence of matches, mismatches, deletions, and/or insertions. For the above reasons, the Court will adopt Invitae's proposed constructions for the following claim terms: "reference alignment" and "sequence read alignments."

D. The "combining" terms

The '799 patent uses the term "combining the contig:reference descriptions with the read:contig descriptions" and the '308 patent uses the term "combining the reference alignment and the sequence read alignments" (collectively, the "combining" terms). The parties' competing proposed constructions for the combining terms are set out in the chart below:

Claim Term	Plaintiff Invitae's Construction	Defendant Natera's Construction
combining the contig:reference descriptions with the read:contig descriptions (the '799 patent) combining the reference alignment and the sequence read alignments (the '308 patent)	"[n]o construction necessary. Plain and ordinary meaning."	"[m]erging the information, including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases, from the 'contig:reference descriptions' / 'reference alignment' with the information, including the position and the existence of matches, mismatches, deletions, and/or insertions for the bases, from the 'read:contig descriptions' / 'sequence read alignments.'"

The parties dispute whether the "combining the contig:reference descriptions with the read:contig descriptions" term in the '799 patent and the "combining the reference alignment and the sequence read alignments" in the '308 patent (collectively, the "combining" terms) should be construed. For the reasons set out below, the Court concludes no construction is necessary.

Natera asserts that the claim language supports its construction. Natera argues that the aim of the "combining step" is "to map positional information of mutations found in the individual reads relative to the reference." *See* '799 patent at claim 1; '308 patent at claims 1, 20. According to Natera, the word "merging" accurately explains the claimed method: "The two datasets are merged together to form a single dataset representing the two inputs." D.I. 80 at 4; *see also* Tr. at 96-97. Natera also relies on the preferred embodiments and examples in the specification to support its construction. D.I. 72 at 94-95. By example, Natera cites to Example 2 which explains that, for the combining step, "[t]he variant information is transferred through to the individual reads by aligning them to the contigs to produce a read:contig BAM file and mapping the first alignment onto the second. The individual reads are thus translated to include the variant and positional information." D.I. 72 at 94 (citing '799 patent at 26:41-46). Natera contends that this

example and other examples and preferred embodiments in the specification of the asserted patents support Natera's construction that the combining step is "merging the positional and variant information from each of the two prior alignment steps to generate a unitary output to map positional information of mutations found in the individual reads relative to the reference." D.I. 72 at 95.

The Court is not persuaded by Natera's arguments and does not see a need to construe the "combining" terms or find any basis to replace "combining" with "merging." Both parties agree that the specification never uses the word "merging" to refer to the invention. D.I. 72 at 91, 95, 98. Further, Natera relies on preferred embodiments and examples found in the specification. "It is [] not enough that the only embodiments, or all of the embodiments, contain a particular limitation. We do not read limitations from the specification into claims; we do not redefine words." *Thorner*, 669 F.3d at 1366.

For the above reasons, the Court concludes no construction is necessary for the combining terms.

V. CONCLUSION

The Court will construe the disputed claim terms as described above, and it will adopt the parties' agreed-upon construction of claim term "genotyping" found in the '308 patent. The Court will issue an Order consistent with this Memorandum Opinion.